Attorney Docket No. 032794-054911 *PATENT*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Gregory H. Altman et al.	Confirmation No.:	6963
Application No.:	10/800,134	Group No.:	1657
Filed:	December 15, 2003	Examiner:	David M. Naff
For:	IMMUNONEUTRAL SILK-FIBER-BASED MEDICAL DEVICES		

SECOND DECLARATION OF DAVID KAPLAN, PH.D. UNDER 37 C.F.R. 1.132

I, David Kaplan, Ph.D., pursuant to 37 C.F.R. § 1.132, hereby declare that:

1. I am currently employed as a Professor and Chair of the Department of Biomedical Engineering at Tufts University. I am also a Professor in the Department of Chemical & Biological Engineering; Director of the Bioengineering & Biotechnology Center; and Director of the Tissue Engineering Resource Center, all at Tufts University.

2. I have authored or co-authored over 350 peer-reviewed publications. Many of the publications involve tissue engineering, silk, and silk-based medical devices. I have over thirty years experience in the field of Natural Biomaterials.

3. A copy of my *Curriculum Vitæ* is attached.

4. I am familiar with the Office Action issued February 8, 2008 by the United States Patent and Trademark Office ("PTO") on Application No. 10/800,134 and the cited U.S. Patents Nos. 7,285,637 (Armato); 6,303,136 (Li); and 5,736,399 (Takezawa).

5. The Office Action contains the following statement:

> "It would have been obvious to omit breaking disulfide bonds as disclosed by Armato et al. if the result of breaking the bonds is not desired, i.e. providing chain fragments which can serve as specific cellular recognition sites promoting attachment and growth of cells since Armato et al disclose that it is possible to merely use degummed silk fibroin fibers to obtain a flexible fabric. It is clear from Armato that fabric can be obtained without breaking the bonds, and omitting breaking the bonds would have been expected to simplify the process and be an advantage. To substitute the advantage of simplification for the advantage of obtaining chain fragments having cellular recognition site promoting attachment and growth of cells would have been within the ordinary skill of the art."

That statement is incorrect, in view of the state of the art as of the filing date of the present application. One skilled in the art would not have made the combination as of the filing date for the following reasons.

6. Armato degums silk fibers and soaks them in a solution of formic acid (col. 2, lines 53-57; col. 3, lines 61-65), which is responsible for partial dissolution of the silk in solution, before developing them into non-woven scaffolds. The resulting scaffold consisted of randomly arranged pieces of formic acid-crosslinked silk fibroin fibers associated with interconnected voids achieved through vacuum dying post evaporation of the acidic solution.

7. Armato does not teach a fabric comprising one or more individual yarns, wherein said yarn comprises one or more sericin-extracted fibroin fibers that retain their native protein structure and have not been dissolved and reconstituted, said fibers being biocompatible and non-randomly organized, wherein said yarn promotes ingrowth of cells around said fibroin fibers and is biodegradable. In fact, Armato teaches essential steps of dissolving (albeit partially) by dissolution in formic acid and reconstituting silkworm fibroin fibers by evaporation and drying. The fibers of Armato do not retain their native protein structure as they have been dissolved purposely to disrupt the disulfide bonds and cross-linked with formic acid. Furthermore, the fibers of Armato are not non-randomly organized but, rather, are purposely randomly organized (see Armato col. 2, lines 58-60 wherein the resulting solution is homogenized and dried; also see Armato Figure 1a).

8. The fibers treated with formic acid solution and the resulting mesh produced by the drying process, as taught by Armato, is incapable of forming a yarn suitable to produce a fabric comprising one or more individual yarns, wherein said yarn comprises one or more sericin-extracted fibroin fibers that retain their native protein structure and have not been dissolved and reconstituted, said fibers being biocompatible and non-randomly organized, wherein said yarn promotes ingrowth of cells around said fibroin fibers and is biodegradable.

9. Armato suggest that "[t]he use of textile methods would theoretically be possible to weave using merely degummed silk fibroin fibers in order to obtain a flexible fabric." (Armato, col. 2, lines 20-22) Armato does not disclose production of or use of fibers that could be used to produce a fabric comprising one or more individual yarns, wherein said yarn comprises one or more sericin-extracted fibroin fibers that retain their native protein structure and have not been dissolved and reconstituted, said fibers being biocompatible and non-randomly organized, wherein said yarn promotes ingrowth of cells around said fibroin fibers and is biodegradable as required by the present claims.

10. For these reasons set forth above, it is my expert opinion that the references cited by the PTO, alone or in combination, would not teach or suggest the claimed invention. The combination or modification of the prior art references in the manner suggested by the PTO was contrary to the accepted wisdom in the art at the time of Applicant's invention and, as discussed above, such combination would render the references inoperable for their intended purposes. One of ordinary skill in the art would not have had a reasonable expectation of success in combining the references suggested by the PTO.

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Date David Kaplan, Ph.D.